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TITLE: A Randomized Controlled Trial of Medical Therapies for Chronic Post-Traumatic Headaches

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14. ABSTRACT

A randomized, placebo-controlled clinical trial is being conducted to evaluate the effectiveness of propranolol, topiramate, and amitriptyline as treatments for chronic post-traumatic headaches secondary to combat-related mild head injury. The study is in the first of three years. 34 of 240 subjects have been enrolled. The study medications are well tolerated. Study subjects had a 60% decrease in headache frequency after 3 months of treatment. There is insufficient data at this time to draw conclusions about the efficacy of specific study medications. The study remains open to enrollment.

15. SUBJECT TERMS
Headache, mild head trauma, treatment

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Introduction

Headaches are the most common symptom after mild traumatic brain injury (1-4). Chronic post-traumatic headaches (PTHAs) develop in 20% of TBI victims, contributing to disability, healthcare utilization, and poor quality of life (5-6). There are no prospective, controlled clinical trials evaluating medical treatments for chronic post-traumatic headaches (7). The purpose of this study is to determine the effectiveness of propranolol, amitriptyline, and topiramate as treatments for chronic PTHAs. We are conducting a single-center, prospective, randomized, double-blind, placebo-controlled, multi-arm trial to evaluate propranolol, amitriptyline, and topiramate for treatment of chronic PTHAs. A total of 240 patients meeting International Classification of Headache Disorders (ICHD) diagnostic criteria for chronic post-traumatic headaches will be enrolled. Subjects are recruited from the Traumatic Brain Injury Program and the Neurology Clinic at Madigan Army Medical Center, Ft. Lewis, WA. Study participants are U.S. Army soldiers with chronic post-traumatic headaches attributable to mild traumatic head injury sustained while deployed to a combat theater. Participants are randomized to receive placebo, propranolol 80 mg daily dose, amitriptyline 50 mg daily dose, or topiramate 100 mg daily dose for 3 months. The primary outcome measure is the number of moderate-severe headache days during the third month of treatment. Secondary outcome measures include the proportion of subjects with at least a 50% reduction in headache frequency, headache-related disability as measured by the Headache Impact Test and Migraine Disability Assessment Scale, PTSD symptom checklist score, and medication side effects. The findings of this study will improve the care of patients with chronic headaches after traumatic brain injury.

Body:

A Physician Assistant was hired in June 2008 and completed all study-related training between June 2008 and September 2008. In September 2008, the study protocol was approved by the MAMC IRB and subject enrollment began. 197 patients were screened for study enrollment between September 2008 and March 2009 and 34 subjects were enrolled. 19 subjects have completed 1 month of study treatment, 14 subjects have completed 2 months of study treatment, and 10 subjects have completed 3 months of study treatment. No adverse events or significant side effects have been reported. Interval analysis of blinded data showed that headache

frequency decreased from 13 days per month during the baseline month to 5 days per month during the third month of treatment. This represents a 60% decline in headache frequency. These data suggest that one or more of the study treatments may be having a beneficial effect on headaches. The study medications have been well tolerated.

The study remains open to enrollment. Enrollment is expected to be relatively slow over the next 12 months, averaging only 2 to 3 new subjects per month, because most troops at Ft. Lewis are deployed. However, enrollment is expected to be very brisk beginning in the summer of 2010 when fifteen thousand troops return to Ft. Lewis.

Key Research Accomplishments:

1. The study protocol was approved by the IRB.
2. A research P.A. was hired and trained.
3. The investigational pharmacy procured identical-appearing study medications and placebo capsules, and developed a system for randomizing, labeling, dispensing, and monitoring study pills.
4. The study has enrolled 15% (34 of 240) of the total projected number of subjects.
5. A study database has been generated.
6. The study continues to enroll new subjects.
7. Interval analysis of blinded data shows improvement of headaches and good tolerability of study medications.

Reportable Outcomes:

There are no reportable outcomes at this time.

Conclusion:

This clinical trial is making progress, having reached 15% of total enrollment during the first 6 months of active enrollment. The study medications have been well tolerated without any adverse events. There is insufficient data at this time to draw meaningful conclusions about the efficacy of specific study medications. However, interval data analysis has shown improvement

of headaches among study participants. Study enrollment will continue for another two years until a total of 240 subjects have been enrolled.

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